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MOUSE *Fkh^{sf}* cDNA SEQUENCE

1 GCTGATCCCC CTCTAGCAGT CCACTTCACC AAGGTGAGCG AGTGTCCCTG
51 CTCTCCCCCA CCAGACACAG CTCTGCTGGC GAAAGTGGCA GAGAGGTATT
101 GAGGGTGGGT GTCAGGAGCC CACCAGTACA GCTGGAAACA CCCAGCCACT
151 CCAGCTCCCG GCAACTTCTC CTGACTCTGC CTTAGACGA GACTTGGAAG
201 ACAGTCACAT CTCAGCAGCT CCTCTGCCGT TATCCAGCCT GCCTCTGACA
251 AGAACCCAAT GCCCAACCCT AGGCCAGCCA AGCCTATGGC TCCTTCCTTG
301 GCCCTTGCC CATCCCCAGG AGTCTTGCCA AGCTGGAAGA CTGCACCCAA
351 GGGCTCAGAA CTTCTAGGGA CCAGGGGCTC TGGGGGACCC TTCCAAGGTC
401 GGGACCTGCG AAGTGGGGCC CACACCTCTT CTTCTTGAA CCCCCTGCCA
451 CCATCCCAGC TGCAGCTGCC TACAGTGCCC CTAGTCATGG TGGCACCCTG
501 TGGGGCCCGA CTAGTCCCT CACCCACCT ACAGGCCCTT CTCCAGGACA
551 GACCACACTT CATGCATCAG CTCTCCACTG TGGATGCCCA TGCCAGACC
601 CCTGTGCTCC AAGTGCGTCC ACTGGACAAC CCAGCCATGA TCAGCCTCCC
651 ACCACCTTCT GCTGCCACTG GGGTCTTCTC CCTCAAGGCC CGGCCTGGCC
701 TGCCACCTGG GATCAATGTG GCCAGTCTGG AATGGGTGTC CAGGGAGCCA
751 GCTCTACTCT GCACCTTCCC ACGCTCGGGT ACACCAGGA AAGACAGCAA
801 CCTTTTGGCT GCACCCCAAG GATCCTACCC ACTGCTGGCA AATGGAGTCT
851 GCAAGTGGCC TGGTTGTGAG AAGGTCTTCG AGGAGCCAGA AGAGTTTCTC
901 AAGCACTGCC AAGCAGATCA TCTCCTGGAT GAGAAAGGCA AGGCCAGTG
951 CCTCCTCCAG AGAGAAGTGG TGCAGTCTCT GGAGCAGCAG CTGGAGCTGG
1001 AAAAGGAGAA GCTGGGAGCT ATGCAGGCCC ACCTGGCTGG GAAGATGGCG
1051 CTGGCCAAGG CTCCATCTGT GGCCTCAATG GACAAGAGCT CTTGCTGCAT
1101 CGTAGCCACC AGTACTCAGG GCAGTGTGCT CCCGGCCTGG TCTGCTCCTC

Fig. 1A



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1101 CGTAGCCACC AGTACTCAGG GCAGTGTGCT CCCGGCCTGG TCTGCTCCTC
1151 GGGAGGCTCC AGACGGCGGC CTGTTTGCAG TCGGAGGCA CCTCTGGGGA
1201 AGCCATGGCA ATAGTTCCTT CCCAGAGTTC TTCCACAACA TGGACTACTT
1251 CAAGTACCAC AATATGCGAC CCCCTTTCAC CTATGCCACC CTTATCCGAT
1301 GGGCCATCCT GGAAGCCCCG GAGAGGCAGA GGACACTCAA TGAAATCTAC
1351 CATTGGTTTA CTCGCATGTT CGCCTACTTC AGAAACCACC CCGCCACCTG
1401 GAAGAATGCC ATCCGCCACA ACCTGAGCCT GCACAAGTGC TTTGTGCGAG
1451 TGGAGAGCGA GAAGGGAGCA GTGTGGACCG TAGATGAATT TGAGTTTCGC
1501 AAGAAGAGGA GCCAACGCCC CAACAAGTGC TCCAATCCCT GCCCTTGACC
1551 TCAAAACCAA GAAAAGGTGG GCGGGGGAGG GGGCCAAAAC CATGAGACTG
1601 AGGCTGTGGG GGCAAGGAGG CAAGTCCTAC GTGTACCTAT GGAAACCGGG
1651 CGATGATGTG CCTGCTATCA GGGCCTCTGC TCCCTATCTA GCTGCCCTCC
1701 TAGATCATAT CATCTGCCTT ACAGCTGAGA GGGGTGCCAA TCCCAGCCTA
1751 GCCCCTAGTT CCAACCTAGC CCCAAGATGA ACTTTCCAGT CAAAGAGCCC
1801 TCACAACCAG CTATACATAT CTGCCTTGGC CACTGCCAAG CAGAAAGATG
1851 ACAGACACCA TCCTAATATT TACTCAACCC AAACCCTAAA ACATGAAGAG
1901 CCTGCCTTGG TACATTGCTG AACTTTCAAA GTTAGTCATG CAGTCACACA
1951 TGACTGCAGT CCTACTGACT CACACCCCAA AGCACTCACC CACAACATCT
2001 GGAACCACGG GCACTATCAC ACATAGGTGT ATATACAGAC CCTTACACAG
2051 CAACAGCACT GGAACCTTCA CAATTACATC CCCCCAAACC ACACAGGCAT
2101 AACTGATCAT ACGCAGCCTC AAGCAATGCC CAAAATACAA GTCAGACACA
2151 GCTTGTCAGA

Fig. 1B



APPROVED BY DRAFTSMAN	O.G. FIG.	
	CLASS	SUBCLASS

MOUSE Fkh^{sf} PROTEIN SEQUENCE

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1  MPNPRPAKPM APSLALGPSP GVLPSWKTAP KGSELLGTRG SGGPFQGRDL
51  RSGAHTSSSL NPLPPSQLQL PTVPLVMVAP SGARLGPSPH LQALLQDRPH
101 FMHQLSTVDA HAQTPVLQVR PLDNPAMISL PPPSAATGVF SLKARPGGLPP
151 GINVASLEWV SREPALLCTF PRSGTPRKDS NLLAAPQGSY PLLANGVCKW
201 PGCEKVFEED EEFLKHCQAD HLLDEKGKAQ CLLQREVVSQ LEQQLELEKE
251 KLGAMQAHLA GKMLAKAPS VASMDKSSCC IVATSTQGSV LPAWSAPREA
301 PDGGLFAVRR HLWGSNGNSS FPEFFHNMDY FKYHNMRRPF TYATLIRWAI
351 LEAPERQRTL NEIYHWFTRM FAYFRNHPAT WKNAIRHNLS LHKCFVRVES
401 EKGAVWTVDE FEFRRKRSQR PNKCSNPCP*
    
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Fig. 2

Docket No. 240083.501D4



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1	GCACACACTC	ATCGAAAAAA	ATTTGGATTA	TTAGAAGAGA	GAGGTCTGCG
51	GCTTCCACAC	CGTACAGCGT	GGTTTTTCTT	CTCGGTATAA	AAGCAAAGTT
101	GTTTTTGATA	CGTGACAGTT	TCCCACAAGC	CAGGCTGATC	CTTTTCTGTC
151	AGTCCACTTC	ACCAAGCCTG	CCCTTGGACA	AGGACCCGAT	GCCCAACCCC
201	AGGCCTGGCA	AGCCCTCGGC	CCCTTCCTTG	GCCCTTGGCC	CATCCCCAGG
251	AGCCTCGCCC	AGCTGGAGGG	CTGCACCCAA	AGCCTCAGAC	CTGCTGGGGG
301	CCCGGGGCCC	AGGGGGAACC	TTCCAGGGCC	GAGATCTTCG	AGGCGGGGCC
351	CATGCCTCCT	CTTCTTCCTT	GAACCCCATG	CCACCATCGC	AGCTGCAGCT
401	GCCCACACTG	CCCCTAGTCA	TGGTGGCACC	CTCCGGGGCA	CGGCTGGGCC
451	CCTTGCCCCA	CTTACAGGCA	CTCCTCCAGG	ACAGGCCACA	TTTCATGCAC
501	CAGCTCTCAA	CGGTGGATGC	CCACGCCCGG	ACCCCTGTGC	TGCAGGTGCA
551	CCCCCTGGAG	AGCCCAGCCA	TGATCAGCCT	CACACCACCC	ACCACCGCCA
601	CTGGGGTCTT	CTCCCTCAAG	GCCCGGCCCTG	GCCTCCCACC	TGGGATCAAC
651	GTGGCCAGCC	TGGAATGGGT	GTCCAGGGAG	CCGGCACTGC	TCTGCACCTT
701	CCCAAATCCC	AGTGCACCCA	GGAAGGACAG	CACCCTTTTCG	GCTGTGCCCC
751	AGAGCTCCTA	CCCACTGCTG	GCAAATGGTG	TCTGCAAGTG	GCCCGGATGT
801	GAGAAGGTCT	TCGAAGAGCC	AGAGGACTTC	CTCAAGCACT	GCCAGGCGGA
851	CCATCTTCTG	GATGAGAAGG	GCAGGGCACA	ATGTCTCCTC	CAGAGAGAGA
901	TGGTACAGTC	TCTGGAGCAG	CAGCTGGTGC	TGGAGAAGGA	GAAGCTGAGT
951	GCCATGCAGG	CCCACCTGGC	TGGGAAAATG	GCACTGACCA	AGGCTTCATC
1001	TGTGGCATCA	TCCGACAAGG	GCTCCTGCTG	CATCGTAGCT	GCTGGCAGCC
1051	AAGGCCCTGT	CGTCCCAGCC	TGGTCTGGCC	CCCGGGAGGC	CCCTGACAGC
1101	CTGTTTGCTG	TCCGGAGGCA	CCTGTGGGGT	AGCCATGGAA	ACAGCACATT

Fig. 3A

Title: IDENTIFICATION OF THE GENE CAUSING THE MOUSE SCURFY PHENOTYPE AND ITS HUMAN ORTHOLOG

Express Mail No. EV207743683US

Inventor(s): Mary E. Brunkow et al. Serial No. 09/697,340 Docket No. 240083.501D4



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1151 CCCAGAGTTC CTCCACAACA TGGACTACTT CAAGTTCCAC AACATGCGAC
1201 CCCCTTTTAC CTACGCCACG CTCATCCGCT GGGCCATCCT GGAGGCTCCA
1251 GAGAAGCAGC GGACACTCAA TGAGATCTAC CACTGGTTCA CACGCATGTT
1301 TGCCTTCTTC AGAAACCATC CTGCCACCTG GAAGAACGCC ATCCGCCACA
1351 ACCTGAGTCT GCACAAGTGC TTTGTGCGGG TGGAGAGCGA GAAGGGGGCT
1401 GTGTGGACCG TGGATGAGCT GGAGTTCCGC AAGAAACGGA GCCAGAGGCC
1451 CAGCAGGTGT TCCAACCCTA CACCTGGCCC CTGACCTCAA GATCAAGGAA
1501 AGGAGGATGG ACGAACAGGG GCCAAACTGG TGGGAGGCAG AGGTGGTGGG
1551 GGCAGGGATG ATAGGCCCTG GATGTGCCCA CAGGGACCAA GAAGTGAGGT
1601 TTCCACTGTC TTGCCTGCCA GGGCCCCTGT TCCCCGCTG GCAGCCACCC
1651 CCTCCCCCAT CATATCCTTT GCCCAAGGC TGCTCAGAGG GGCCCCGGTC
1701 CTGGCCCCAG CCCCCACCTC CGCCCCAGAC ACACCCCCCA GTCGAGCCCT
1751 GCAGCCAAAC AGAGCCTTCA CAACCAGCCA CACAGAGCCT GCCTCAGCTG
1801 CTCGCACAGA TTA CTTCAGG GCTGGAAAAG TCACACAGAC ACACAAAATG
1851 TCACAATCCT GTCCCTCAC

Fig. 3B

Title: IDENTIFICATION OF THE GENE CAUSING THE MOUSE SCURFY PHENOTYPE AND ITS HUMAN ORTHOLOG

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	CLASS	

HUMAN FKHS^{sf} PROTEIN SEQUENCE

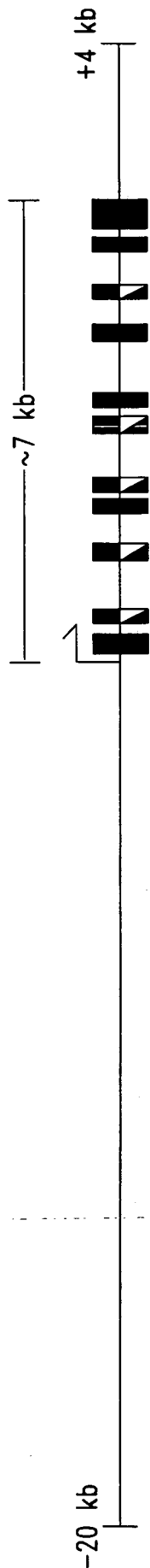
1 MPNPRPGKPS APSLALGPSP GASPSWRAAP KASDLLGARG PGGTFQGRDL
51 RGGAHASSSS LNPMPPSQLQ LPTLPLVMVA PSGARLGPLP HLQALLQDRP
101 HFMHQLSTVD AHARTPVLVQ HPLESPAMIS LTPPTTATGV FSLKARPGLP
151 PGINVASLEW VSREPALLCT FPNPSAPRKD STLSAVPQSS YPLLANGVCK
201 WPGCEKVFEED PEDFLKHCQA DHLLDEKGRA QCLLQREMVQ SLEQQLVLEK
251 EKLSAMQAHLE AGKMALTKAS SVASSDKGSC CIVAAGSQGP VVPAWSGPPE
301 APDSLFAVRR HLWGSHGNST FPEFLHNMDY FKFHNMRPPF TYATLIRWAI
351 LEAPEKQRTL NEIYHWFTRM FAFFRNHPAT WKNAIRHNLS LHKCFVRVES
401 EKGAVWTVDE LEFRKKRSQR PSRCSNPTPG P*

Fig. 4



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Vector for generation of FKH^{sf} Transgenic mice



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Fig. 5



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FKHsf Transgene corrects the defect in
scurfy animals

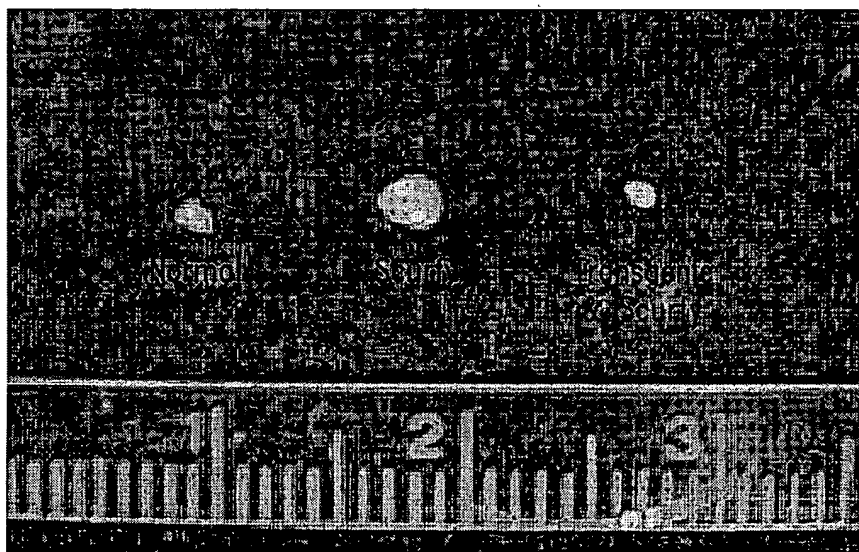


Fig. 6



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FKHsf tg mice have reduce lymph node cells
compared to normal cells

Cell number	Mouse genotype		
	Normal	Scurfy	Transgenic
Cells / LN	0.92	1.97	0.29
Cells / Thymus	0.76	0.54	0.76

Fig. 7

FKHsf transgenic mice respond poorly to in vitro stimulation

Proliferation	Mouse genotype		
	Normal	Scurfy	Transgenic
No stimulation	778	23488	596
Anti-CD3+Anti-CD28	22932	225981	9106

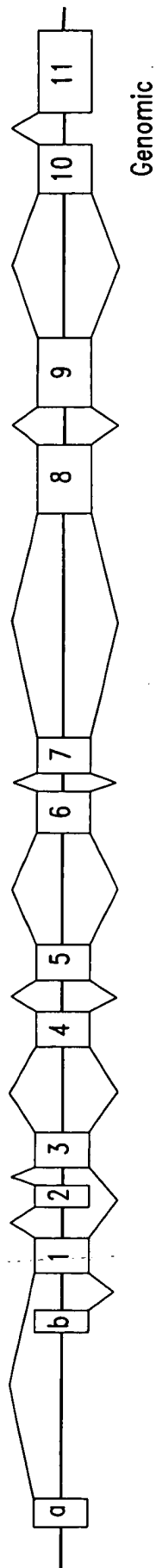
Fig. 8



APPROVED	O.G. FIG.	
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a 1 2 3 4 5 6 7 8 9 10 11 FKHS^{sf} cDNA

b 1 3 4 5 6 7 8 9 10 11 JM2 cDNA



Comparison of FKHS^{sf} and JM2 cDNAs. Exon/intron structure is shown (Genomic) as open rectangles (exons) joined by heavy horizontal lines (introns). Coding exons are numbered 1-11 as determined by sequence analysis of FKHS^{sf} cDNA; non-coding 5' exons are labelled *a* and *b*. The FKHS^{sf}-specific and JM2-specific splicing patterns and resulting cDNAs are indicated above and below the genomic structure, respectively.

Fig. 9

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Human FKHSf		Mouse Fkh ^{sf}	
N-terminal	Mid	Forkhead	
83.4%	82.8%	96.4%	

Human and mouse FKHSf proteins are highly conserved.

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Fig. 10